

Elazar Rabbani et al.
Serial No.: 08/978,637
Filed: November 25, 1997
Page 7 [Amendment Under 37 C.F.R. § 1.115 (In Response
to the February 16, 1999 Office Action - August 17, 1999)]



REMARKS

Reconsideration of this application is respectfully requested.

Claims 2-24 and 245-313 were previously pending in this application. Claims 2-24 have been canceled. Claims 247, 249, 251, 253-254, 256, 259, 268, 273, 278-279, 283, 289, 302-303 and 312 have been amended above. No claims have been added. Accordingly, claims 245-313 as amended are presented for further examination.

The first page (line 1) of the specification has been amended by inserting information cross-referencing this divisional application with the prior parent application, Serial No. 08/574,443, filed on December 15, 1995. The parent application was revived for purposes of continuity so that the present divisional application could be filed.

Several informalities in the specification have been corrected. These include changes on pages 9, 64, 81, 105, 109, 114, 123, 127, 134, 151, 159, 180 and 181, none of which is believed to have inserted new matter into Applicants' disclosure. Referring to the aforementioned page 81 (line 7), Applicants have corrected the description of an incompatible cell to mean "a cell *incapable* of processing RNA by removal of the processing element." The definition of an incompatible cell is in contrast to the definition of a compatible cell that precedes it. In the preceding lines on page 81, a compatible cell is defined as "a cell capable of processing RNA by removal of the processing element." See page 81, lines 5-6. In clarifying the definition of an incompatible cell, Applicants have corrected an obvious error in the specification that is clear from its context. Thus, no new matter has been inserted thereby.

For the sake of clarity and definiteness, relatively minor changes have been made to seventeen claims above. The inadvertent redundancy in claims 247, 278 and 302 with respect to the second occurrence of "a phage" has been deleted. Another redundancy in claim 265 (penultimate line) with respect to the word "localizing" has also been deleted. It is believed that the

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foregoing changes to claims 247, 265, 278 and 302 either meet the Examiner's requirements, adopt her suggestions for claim clarity or otherwise improve the clarity of these claims.

Minor changes have also been made to sixteen claims, including claims 247, 249, 251, 253, 254, 256, 259, 268, 273, 278, 279, 283, 289, 302, 303 and 312. These other minor changes affect only the Markush language in the foregoing claims. It is believed that the amended claim language in these claims conforms to the accepted proper usage under U.S. patent practice.

Entry of the above amendments to the specification and claims is respectfully requested.

Objection to Patent Drawings

Acknowledgement is made of the Notice of Draftperson's Patent Drawings Review that was issued in connection with this application. Formal drawings will be submitted as soon as allowable subject matter has been indicated in this application.

Submission of Sequence Listing

Applicants are filing concurrently with this Amendment a response to the Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

The Rejection for Double Patenting Under 35 U.S.C. §101

Claims 2-24 stand provisionally rejected under 35 U.S.C. §101 as claiming the same invention as that of claims 2-24 of copending Application Nos.: 08/978,632, 08/978,633, 08/978,634, 08/978,635, 08/978,636, 08/978,638, 08/978,639, and 08/574,443. As indicated by the Examiner

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on page 2 of the February 17, 1999 Office Action, "This is a provisional double patenting rejection since the conflicting claims have not in fact been patented."

As indicated above, claims 2-24 have now been canceled as they should have been when claims 245-313 were presented in Applicants' November 25, 1997 Preliminary Amendment. Any inconvenience caused by this oversight is sincerely regretted.

In view of the cancelation of claims 2-24, Applicants respectfully request withdrawal of the double patenting rejection

The Rejection Under 35 U.S.C. §112, Second Paragraph

Claims 2-21 and 265 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the Office Action (page 3), the Examiner stated:

Claims 2-21 are indefinite because they depend from canceled claim 1. Therefore, claims 2-21 do not depend on any independent claim.

Claim 265 contains the redundant language "localizing localizing entity"

The Examiner's comments above have been well taken with respect to claims 2-21 and 265, leading to the cancelation of the former claims, including claims 22-24, and amendment of the latter claim (see the opening remarks of this Amendment).

In light of the cancelation of claims 2-24 and the above amendments to claim 265, it is respectfully requested that the rejection under 35 U.S.C. §112, second paragraph, be reconsidered and withdrawn.

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The Rejection Under 35 U.S.C. §112, First Paragraph

Claims 2-21 and 245-313 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In the Office Action (pages 3-4), the Examiner stated:

The constructs taught in the claims 2-24 are broadly drawn to a multitude of possible nucleic acid based constructs for use in a cell to produce a product (and in any context, *in vivo* or *in vitro*), comprising: (1) the construct as linear or circular, (2) the construct as comprising 1,2 or 3 strands, (3) comprising a terminus, a polynucleotide tail which can hybridize, (4) composed of RNA or DNA or combinations, (5) containing chemically modified nucleotides or analogs, (6) containing non-nucleic acid entities composed of polymers or ligands or a combination, (7) further specifying the natural and synthetic polymers, the synthetic homo- or heteropolymer with a net charge, (8) the construct imparting a "further biological activity" by the modified nucleotide, analog, entity, ligand or combination of those, further defined as nuclease resistance, cell recognition, cell binding, and cellular or nuclear localization or a combination, (9) a ligand attached to one of the modified nucleotides, etc. of claim 1, further described as attached to a "segment" or "tail" of the construct, and further defined as being a macromolecule or small molecule or combination. Claims 22-24 describe a second construct "which when present in a cell produces a product, said construct being bound non-ionically to an entity comprising a chemical modification or a ligand."

Claims 245-264 are drawn to nucleic acid compositions and cells containing them. Specifically, a composition for producing a primary, secondary and tertiary nucleic acid component independently obtained in the cell. The limitations further are drawn to a signal processing sequence in the composition such as a promoter, initiator, terminator, intron or cellular localization element. Claims 265-289 are drawn to compositions comprised of a nucleic acid component and producing in a cell a non-natural nucleic acid product further comprising a portion of a localizing entity, and cells and organisms for use in. The limitations of the dependent claims are further drawn to nuclear localized RNA comprising snRNA such as U1 or U2. Claims 290-298 are drawn to a process for localizing the above claimed composition in claims 265-289. Claims 299-313 are drawn to a nucleic acid component capable of producing more than one non-homologous nucleic acid sequence in a cell complementary to a target nucleic acid or protein. The dependent limitations include use of a localizing protein (claim 310).

The Examiner's comments continued on pages 5-7:



The specification teaches several constructs designed for entry into a cell and expression of one or more sequences to perform a biological function such as antisense inhibition of a nucleic acid. Specifically, several CHENAC constructs are taught prophetically, and pictured in figures 1-13 as vector based constructs constructed by using modified nucleic acid regions and designed to provide improved entry into a cell by way of improved construct-cell interaction. A second group of nucleic acid fused with antibody based constructs are taught prophetically and shown in figures 14-21. Preparation of multimeric insulin by means of nucleic acid hybridization is further taught prophetically and shown in figures 22-23. No exemplification for such constructs is taught in the specification as filed.

Furthermore, vectors ultimately designed for antisense inhibition of HIV in cells by co-expression of antisense DNA under control of a T7 promoter with a T7 polymerase (represented in figures 24-49) are taught and supported by *in vitro* data. Specifically, construction of the M13 phage vectors pRT-A, pRT-B, and pRT-c are taught which contain the coding sequence for the T7 RNA polymerase driven by the RSV promoter and with an SV40 intron sequence that will be spliced out to form a functional polymerase enzyme and each respective construct also having the antisense A, B, and C sequences driven by a T7 promoter and terminated by a T7 terminator. A modified version of the pINT-3 construct (the parent vector of pRT-A, B and C vectors before insertion of the antisense sequences) is taught where a polylinker is inserted behind the poly-A tail of the T7 polymerase gene for subsequent sub-cloning of the lacZ gene in this instance to form pINT-LacZ. The result upon introduction in a eukaryotic cell would be synthesis of the T7 polymerase from the RSV promoter which in turn acts upon the T7 promoter to synthesize B-galactosidase.

Furthermore, plasmids are taught containing anti-sense segments introduced into the transcript region of the U1 gene, plasniid pHSD-4 U1 so that upon expression of the transcript, the antisense RNA sequence is produced to the complementary region of the HIV genome. Specifically, pDU1 -A, B, C and D were made using the antisense A, B, and C sequences previously described and D as a control containing a non-HIV sequence. A multi-cassette version of the constructs was also made by sub-cloning in tandem the A,B, and C antisense to make pNDU1 (A,B,C) (N meaning the construct was also contained the gene for neomycin resistance).

Other multi-cassette constructs taught were:

(1) TRI 101, an M13 phage vector containing the "A" antisense T7 operon, the "B" antisense T7 operon and the "C" antisense T7 operon in a single construct (figure 46). Co-transfection would be required for expression of the antisense molecules from this construct with a vector that expresses T7 RNA polymerase (suggested is the intron containing construct of example 19); and,

(2) an M13 construct constructed from a multi-ligation of portions of pINT-3 (containing the intron containing polymerase) and the T7 promoter driven A, B, and C sequences (see figure 47).

The specification teaches application of some of these constructs ("various U1 constructs described above" p. 167, last line) in antisense inhibition of HIV in infected U937 cell culture. Specifically

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the following is shown: (1) expression of A, B, and C antisense by hybridization analysis after expression of the "U1 clone" (p. 169, line 3), (2) expression of the "triple U1 construct" (p. 169, para. (c), line 1) which result in a decrease in p24 production next to the control, and increased % reduction in p24 over time and after re-infection of cells, and these results were confirmed by absence p24 amplification next to control cells via PCR of the targeted DNA, and (3) expression of the construct of figure 50, a fusion product antisense A upstream of B-gal gene where antisense activity of the A portion caused inhibition of B-gal activity as shown in lacZ assays. The results in figure 51 show HIV A/Anti-A activity and HIV A/Anti-ABC (when the triple U1 construct was used by *co-transfection*) as the equivalent of the uninfected cells whereas the infected and control containing cells showed high B-gal expression. Therefore, it does not appear in the specification as filed that the multicassette A,B,C and T7 polymerase construct (expressed on same plasmid) was applied to the same HIV challenge experiments.

Additional constructs are more prophetically taught: the primary nucleic acid construct that propagates production centers for the production of single-stranded antisense, etc. in examples 21-25, and the retrovirus vector containing sequences for the expression of antisense RNA directed at HIV on page 181, last para.

In the Office Action (pages 7-10), the Examiner further stated:

Claims 22-24 read on any construct bound non-ioniically to a ligand or otherwise chemically modified entity, further limited as having a polynucleotide tail terminus and where the tail is hybridized to a complementary polynucleotide sequence. The breadth of genus sought for such is not enabled in view of the lack of specificity of guidance in the specification as filed. The specification fails to provide guidance for the breadth claimed since the claims vaguely claim "constructs" which "produce products." The specification teaches only by way of example HIV inhibition by antisense expression from vector constructs which do not entail chemical modified entities nor polynucleotide termini.

Claims 245-313 are further drawn to a broad genus of constructs and processes of using such constructs in cells. The language of claim 245 reads on vector replication in a cell, and expression of any gene which is then modified (spliced, etc.) so that a third nucleic acid sequence is produced, or acts on another nucleic acid sequence such as a ribozyme to cleave the product. The language of claim 265 and 290 reads on any construct and process for production of a recombinant nucleic acid in a cell having a localizing entity, for example to localize the expressed sequence to its target region. The language of claim 299 reads on any construct for production of nucleic acid sequences in a cell which target another nucleic acid sequence or protein in the cell.

The scope of genus sought for such constructs is not enabled in view of the lack of specificity of guidance in the specification as filed. The specification fails to provide guidance for the breadth claimed.



since the claims nebulously claim "construct" which produce "products" having general characteristics of a huge genus of recombinantly expressed nucleic acid products in a cell of interest. The specification does not teach compositions producing primary, secondary, tertiary (or the production of more than one sequence as in claim 299) constructs, other than the triple U1 construct having a cassette structure. The only localizing entity shown by way of example in the specification is the use of the U1 sequence for direction of the antisense sequences to the nucleus. The specification teaches only prophetically constructs capable of binding to a specific protein of interest in the cell, and by way of example, only vectors such as the U1A,B,C construct for expression of antisense to HIV in cells.

level of unpredictability in the antisense art and analogous gene therapy art for *in vivo* (whole organism) applications. The factors considered barriers to successful delivery of antisense delivery to the organism are: (1) penetration of the plasma membrane of the target cells to reach the target site in the cytoplasm or nucleus, (2) withstanding enzymatic degradation, and (3) the ability to find and bind the target site and simultaneously avoid non-specific binding (see Branch). Despite the synthesis of more resilient, nuclease resistant, oligonucleotide backbones and isolated successes with antisense therapy *in vivo*, the majority of designed antisense molecules still face the challenge of successful entry and localization to the intended target and further such that antisense and other effects can routinely be obtained. Note Flanagan et al. who teach "although numerous reports have cited antisense effects using oligonucleotides added to cell medium, direct proof that oligonucleotides enter cells and affect gene inhibition by an antisense mechanism is still lacking (page48, column 1)."

Specifically, *in vitro* results with one antisense molecule are not predictive of *in vivo* (whole organism) success. *In vitro*, antisense specificity to its target may be manipulated by "raising the temperature or changing the ionic strength, manipulations that are commonly used to reduce background binding in nucleic acid hybridization experiments." (Branch, p. 48) Discovery of antisense molecules with "enhanced specificity" *in vivo* requires further experimentation for which no guidance is taught in the specification. Note Branch who teaches the state of the art for designing an antisense which inhibits a target *in vivo*: it "is very difficult to predict what portions of an RNA molecule will be accessible *in vivo*, effective antisense molecules must be found empirically by screening a large number of candidates for their ability to act inside cells (Branch, p.49)." And in the instant case, the claims read broadly on administration of an antisense inhibitor in any cell, therefore the whole organism included. While the specification teaches cell culture inhibition, no evidence of successful *in vivo* (whole organism) antisense inhibition has been shown, nor do the culture examples correlate with whole organism delivery.

The Examiner's comments on enablement were concluded on pages 10-11:

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One of skill in the art would not accept on its face the successful delivery of the disclosed antisense molecules *in vivo* in view of the lack of guidance in the specification and the unpredictability in the art. Specifically the specification does not teach (1) stability of the antisense molecule *in vivo*, (2) effective delivery to the whole organism and specificity to the target tissues, (3) dosage and toxicity, nor (4) entry of molecule into cell and effective action therein marked by visualization of the desired treatment effects. These key factors are those found to be highly unpredictable in the art as discussed *supra*. The lack of teaching of these factors in inhibition of the target, coupled to the amount of "trial and error" experimentation involved in the deduction of these results would lead one skilled in the art to necessarily practice an undue amount of experimentation *in vivo*.

No determination of enablement can be made for claims 2-21 because there is no independent claim from which they depend. Without knowing what claims 2-21 depend on, the full scope of the claims is not known.

The enablement rejection is respectfully traversed.

With respect to the application of the enablement rejection to claims 2-24, such grounds have been rendered moot, of course, by the cancelation of these claims.

With respect to claims 245-313, it is respectfully submitted that the subject matter of these claims is fully enabling such that a person skilled in the art could practice, without undue experimentation, Applicants' claimed invention. It is respectfully submitted that the ordinarily skilled artisan, armed with the disclosure, could practice the composition, localizing process and nucleic acid component set forth in the present claims.

Reconsideration and withdrawal of the enablement rejection are respectfully requested.

The Rejection Under 35 U.S.C. §112, First Paragraph

Claims 2-24, 245-289 and 299-313 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in



the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the Office Action (pages 11-13), the Examiner stated:

Claims 2-21 are drawn to a missing independent claim and therefore the scope claimed is not able to be determined. Claims 22-24 are drawn to a broad scope of constructs which are bound non-ionically to an entity having a chemical modification or a ligand and produce a product in a cell. Claims 245-289 and 299-313 are drawn to a broad scope of (1) compositions for production of primary, secondary and tertiary nucleic acid products in a cell, (2) nucleic acid compositions comprising localizing entities, and (3) nucleic acid compositions for producing a sequence homologous to an endogenous cell sequence or protein.

The claims broadly encompass "constructs" for producing a "product" and it is not clear what is embraced by the claims. The claims 22-24 read on vectors, genomes, cell processes like translation, transcription, etc. Furthermore, the scope of "chemical modification" as used in claim 22 is not clear in relation to the construct. Claims 245-289 and 299-313 read on vector replication in a cell, expression of any recombinant gene with a signal sequence or any such sequence that would direct it to a specific location or any sequence to target another nucleic acid or protein in the cell.

The instant specification describes prophetically a number of potential modified nucleic acid constructs for expression of an entity in a cell. The supporting figures provide limited additional disclosure of relevant identifying structural characteristics because they primarily correspond to expression vector based constructs which are only one facet of the invention in light of the nebulous scope claimed.

Clearly the specification only considers vector-like constructs for delivery and expression of nucleic acids. Specifically, for claims 245-289 and 299-313, the only localizing entity taught is use of the U1 gene with an internal antisense sequence for localization of the antisense to the nucleus once expressed in the cell. Further, the only primary, secondary, and tertiary product producing construct described in the specification is the cassette structured 'triple U1' construct and with the use of intron sequences the control of processing of the T7 polymerase taught.

Furthermore, the actual constructs used in the HIV challenge and Lac-Z assays taught in the specification are not described in clear and exact terms (p. 169, line 3 recites "U1 clone"; p. 169, para. @ line 1 recites "triple U1 construct"; and p. 167, last line recites "various U1 constructs described above") and it is not clear whether the constructs used had the intron sequence in the T7 polymerase, or even which constructs were used in the assays.

Despite the known predictability of standard vector construction in the molecular biology art, in view of the nearly infinite scope claimed and the lack of adequate description in the specification for such a broad genus of possible "constructs," coupled with the high

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level of unpredictability for constructs which could fall within this genus such as those involving gene therapy, the specification as filed fails to provide one skilled in the art enough description to show possession of a representative number of "construct" species for the breadth claimed.

See the June 15, 1998 (Vol. 63, No. 114, Pages 32639-32645) Federal Register for the interim guidelines for the examination of patent applications under the 35 U.S.C. 112 "Written Description" requirement.

The written description rejection is respectfully traversed.

With respect to claims 2-24, the cancellation of those claims above renders the instant description rejection moot as it applies to the now canceled claims.

With respect to claims 245-313, it is believed that the scope of these claims is of proper breadth and scope so as to reasonably convey to one skilled in the relevant art that the present inventors had possession at the time this application was first filed in December 1995 of the same matter now being claimed.

Reconsideration and withdrawal of the written description rejection are respectfully requested.

The First Rejection Under 35 U.S.C. § 102

Claims 22-24 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Meyer et al., U.S. Patent No. 5,574,142, issued on November 12, 1996, based upon an application filed on December 15, 1992. In the Office Action (page 14), the Examiner stated:

The claimed invention is drawn to any construct which when present in a cell produces a product, and is bound non-ionically to an entity comprising a modification or a ligand, and further comprises a hybridized polynucleotide tail.

Meyer et al. teach a covalently linked conjugate of an oligonucleotide (ODN) with a peptide and a carrier or targeting ligand (ODN-peptide-carrier) including a therapeutic oligonucleotide which is capable of selectively binding to a target sequence of DNA, RNA or protein inside a target cell. The invention of Meyer et al. Reads on all of the instant claim limitations for a non-naturally occurring

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construct for production of a product in a cell (in Meyer, an antisense oligonucleotide is produced).

With the cancelation of claims 2-24 above, it is believed that the anticipation rejection based upon Meyer's patent has been rendered moot.

Reconsideration and withdrawal of this anticipation rejection are respectfully requested.

The Second Rejection Under 35 U.S.C. §102

Claims 265-298 stand rejected under 35 U.S.C. §102(e) as being anticipated by Sullenger et al., U.S. Patent No. 5,584,038, issued on December 29, 1998, based upon an application filed on January 22, 1993. In the Office Action (page 14), the Examiner stated:

The claimed invention is drawn to construct and methods of use of a construct for production of a non-naturally occurring nucleic acid product in a cell comprising a portion of a localizing entity in a cell.

Sullenger et al. teaches, for example, nucleic acid constructs for production in a cell of ribozyme sequences tethered to a localization signals. Although Sullenger does not specifically teach snRNA, U1 or U2, localization signals, many other nuclear localization signals are taught as having improved specificity to the particular target site of interest (his examples are also drawn to HIV targets). Sullenger et al. also encompass use of protein binding nucleic acid sequences.

The anticipation rejection based on Sullenger is respectfully traversed.

Applicants respectfully contend that there is a lack of material identity between their claimed elements and Sullenger's disclosure.

Reconsideration and withdrawal of the rejection is respectfully requested.

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The Third Rejection Under 35 U.S.C. §102

Claims 245-249, 251, 255, 258-261, and 264 stand rejected under 35 U.S.C. §102(b) as being anticipated by Huse et al., U.S. Patent No. 5,128,256, issued on July 7, 1992, based upon an application filed on January 12, 1987. In the Office Action (page 15), the Examiner stated:

The claimed invention is drawn to a composition comprising a primary nucleic acid component which upon introduction into a cell produces a secondary nucleic acid component which is capable of producing a nucleic acid product, or a tertiary nucleic acid component, wherein the primary nucleic acid component is not obtained with the secondary or tertiary component.

Huse et al. teach the Lambda ZAP vector known in the art for expression of a second vector after transformation into the cell having the potential to subsequently express a product. Claim 245 as written, however, would literally read on any generic propagating vector in a cell.

The anticipation rejection by Huse et al. is respectfully traversed.

It is respectfully contended that Huse's patent neither discloses nor suggests Applicants' claimed invention. Reconsideration and withdrawal of this anticipation rejection is respectfully requested.

The Fourth Rejection Under 35 U.S.C. §102

Claims 245-264 and 299-313 stand rejected under 35 U.S.C. §102(e) as being anticipated by Giri et al., U.S. Patent No. 5,604,118, issued on February 18, 1997, based an application filed on June 18, 1990. In the Office Action (page 15), the Examiner stated:

Claim 245 is drawn to a composition comprising a primary nucleic acid component which upon introduction into a cell produces a secondary nucleic acid component which is capable of producing a nucleic acid product, or a tertiary nucleic acid component, wherein the primary nucleic acid component is not obtained with the secondary or tertiary component. Claim 299 is drawn to nucleic acid construct which when in a cell produces more than one non-homologous nucleic acid sequence with complementarity to a target nucleic acid or protein.

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Giri et al. teach a eukaryotic expression vector for simultaneous expression of a sense and an antisense sequence from different promoters (see column 3). Targeting different viral sequences (protein or nucleic acid) is within the scope of the vectors as taught.

The anticipation rejection by Giri et al. is respectfully traversed.

It is believed that Giri's disclosure does not anticipate the present invention.

Reconsideration and withdrawal of the fourth anticipation rejection are respectfully requested.

The Fifth Rejection Under 35 U.S.C. §102

Claims 245-313 stand rejected under 35 U.S.C. §102(b) as being anticipated by DeYoung et al., ["Functional Characterization of Ribozymes Expressed Using U1 and T7 Vectors for the Intracellular Cleavage of ANF mRNA," Biochemistry 33:12127-12138 (1994)]. In the Office Action (page 16), the Examiner stated:

The claimed invention is drawn to: (1) compositions for production of primary, secondary and tertiary nucleic acid products in a cell, (2)nucleic acid compositions comprising localizing entities, and (3)nucleic acid compositions for producing a sequence homologous to an endogenous cell sequence or protein.

DeYoung et al. teach expression of ribozymes imbedded in a U1 sequence and under the control of a T7 promoter. The U1 sequence is a known localizing sequence to the cell nucleus. The production of ribozymes from the construct taught by DeYoung reads on the broad genus of constructs for production of secondary and tertiary nucleic acid products and compositions for producing a sequence homologous to an endogenous cell sequence.

The anticipation rejection based upon DeYoung's publication is respectfully traversed.

Applicants maintain that the anticipation rejection cannot reasonably be maintained due to a lack of identity in material elements set forth in claims 245-313 and DeYoung's disclosure.

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Reconsideration and withdrawal of the fifth anticipation rejection is
respectfully requested.

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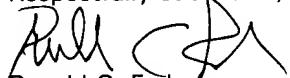
SUMMARY AND CONCLUSIONS

Claims 245-313 are being presented for further examination, with claims 2-24 having been canceled and claims 247, 249, 251, 253, 254, 256, 259, 268, 273, 278, 279, 283, 289, 302, 303 and 312 having been amended above.

This Amendment is being accompanied by a Request For An Extension Of Time (3 months) and authorization for the small entity fee therefor. No other fee or fees are believed due for filing this Amendment. In the event that any other fee or fees are due, however, authorization is hereby given to charge the amount of any such other fee(s) to Deposit Account No. 05-1135, or to credit any overpayment thereto.

If a telephone conversation would further the prosecution of the present application, Applicants' undersigned attorney request that he be contacted at the number provided below.

Respectfully submitted,


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